

## REMARKS

In the Office Action, claims 33-36 are rejected under 35 U.S.C. §103 as allegedly unpatentable over U.S. Patent No. 5,252,295 (Gluchowski) in view of any of U.S. Patent No. 5,981,563 (Lowrey), U.S. Patent No. 5,942,545 (Samour), and U.S. Patent No. 5,236,904 (Gerstenberg). Claim 33 has been amended. Applicants believe that the rejection should be withdrawn at least in view of the amendment and the reasons set forth below.

Of claims 33-36, claim 33 is the sole independent claim which has been amended as previously provided. Claim 33 recites an ophthalmic formulation in aqueous solution for topical administration including a sterile aqueous carrier; and a pharmaceutically active compound consisting essentially of phentolamine in a therapeutically effective amount to contract a pupil of a human patient's eye in dim light so that the pupil is effectively reduced to improve vision in dim light and further to minimize eye redness. Support for the amendment can be found in Applicant's specification, for example, on pages 18 to 20 in Examples 1 and 2. Claims 34-36 depend from claim 33.

At the outset, Applicant respectfully requests the Patent Office to reconsider Applicant's position that the primary reference (e.g., Gluchowski) and the secondary references (e.g., Lowrey, Samour et al and Gerstenberg) are not combinable. In the Office Action, the Patent Office alleges that "[m]otivation was provided based on a disclosure that was present in any of the secondary references...". See, Office Action, page 2. Contrary to the Patent Office position, Applicant does not believe "it can be reasonably expected that motivation to use the compound [e.g., phentolamine] will be present in the secondary references.". See, Office Action, page 2.

While the secondary references disclose phentolamine, these disclosures are directed to an entirely different application (e.g., treatment of sexual dysfunction; See generally, secondary references) as compared to a method for reducing or maintaining intraocular pressure in the mammalian eye as provided in Gluchowski. Further, the secondary references are directed to different formulations that require different routes of administration (e.g., intracavernosal injection of a peptide N-terminal histidine C-terminal methionine amide (Gerstenberg Abstract); oral administration in tablet form (Lowrey Abstract); and topical transdermal administration prostaglandin E, active ingredient in an aqueous alcoholic carrier (Samour Abstract)). Moreover, the Patent Office cannot properly rely on Applicant's disclosure in further support of the alleged combinability of the primary and secondary references as the Patent Office continues to do. See,

Office Action, page 4. Again, “[t]here must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the combination. That knowledge can not come from the applicant’s invention itself.” See, *In re Oetiker*, 24 USPQ2d 1443, 1446 (Fed. Cir. 1992). Therefore, Applicant submits one skilled in the art would recognize that the differences (e.g. application, formulation type, and route of administration) between the subject matter of the primary and secondary references are too great, thus making the references wholly unrelated and rendering the combinability thereof unpredictable and improper.

Even assuming that the references are properly combinable, Applicant believes that the alleged combined teachings fail to teach or suggest the claimed invention. At the outset, the Patent Office seems to have alleged that Gluchowski renders the limitation (e.g., consisting essentially of phentolamine) obvious. See, Office Action, paragraph 2, page 2. However, this position is inconsistent with the obviousness rejection in that the secondary references are cited in combination with Gluchowski. See, Office Action, page 3, paragraph 3. Further, the Patent Office again alleges that Gluchowski “does not teach a pharmaceutically active compound consisting essentially of phentolamine”. *Id.* Clearly, this suggests that Gluchowski, on its own, fails to anticipate or render obvious the claimed invention. If the Patent Office believes that Gluchowski on its own can be asserted against the presently pending claims, then a new rejection should be asserted instead of the presently asserted rejection that alleges the combinability of the Gluchowski and any one of the listed secondary references in support thereof.

In any event, Applicant believes that Gluchowski on its own and even if properly combinable with the secondary references fails to render obvious the claimed invention. As previously discussed, the claimed invention is directed to an ophthalmic formulation in aqueous solution for topical administration with an active phentolamine compound that can effectively reduce pupil size in dim light to improve vision in dim light and further minimize redness in the eye upon use. Applicant has conducted experiments as detailed in the specification which demonstrate the enhanced benefits to vision in dim light associated with the claimed phentolamine-based formulation as compared to other alpha-1 antagonist-based formulations. See, Published Specification (US2004/0176408), Examples 1 and 2 and Tables 1 and 2, beginning on page 6. Moreover, such unexpected results are further supported by an Affidavit of

Gerald Horn, M.D. that was submitted in related patent application No. 09/854,414, a copy of which is attached herewith for consideration.

At best, Gluchowski indicates that oxazoline or imidazoline compounds are preferred (See, Gluchowski, col. 3, lines 39-41), but nowhere does Gluchowski specify an ophthalmic formulation that includes a pharmaceutically active compound consisting essentially of phentolamine and in a therapeutically effective amount to contract a pupil of a human patient's eye in dim light so that the pupil is effectively reduced to improve vision in dim light and further to minimize eye redness as required by the claimed invention. Indeed, Gluchowski is directed to intraocular pressure and not reduction in pupil size, let alone the reduction of pupil size in dim light to improve vision in dim light where redness is further minimized as required by the claimed invention. Moreover, the secondary references fail to recognize the unexpected benefit of phentolamine in an ophthalmic formulation, let alone a phentolamine-based ophthalmic formulation in aqueous solution for topical administration that can effectively reduce pupil size in dim light to improve vision. Again, the secondary references are directed to the treatment of sexual dysfunction and further relate to different types of formulations that require different routes of administration. Therefore, Applicants believe that the Patent Office has failed to establish a *prima facie* case of obviousness, and thus respectfully request that the obviousness rejection be withdrawn in view of same.

Applicant notes that a supplemental information disclosure statement (IDS) is being submitted concurrently with this Response. A request for continued examination along with the requisite fees are also being submitted concurrently with this Response to ensure entry and examination of the supplemental IDS and further to ensure timely entry of this Response for examination purpose. The Commissioner is hereby authorized to charge deposit account 02-1818 for any fees which are due and owing.

For the foregoing reasons, Applicant respectfully submits that the present application is in condition for allowance and earnestly solicits reconsideration of same.

Respectfully submitted,

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